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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/537,784

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Michal Amit

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09/15/2008

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EXAMINER

CROUCH, DEBORAH

ART UNIT

PAPER NUMBER

1632

MAIL DATE

DELIVERY MODE

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/537,784	Applicant(s) AMIT ET AL.	
	Examiner Deborah Crouch, Ph.D.	Art Unit 1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 28 May 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 153-179 and 181-237 is/are pending in the application.
- 4a) Of the above claim(s) 218-220 is/are withdrawn from consideration.
- 5) ☒ Claim(s) 229 is/are allowed.
- 6) ☒ Claim(s) 153-179, 181-217, 221-228 and 230-237 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 06 June 2005 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>8/15/08</u> . | 6) <input type="checkbox"/> Other: _____ |

Applicant's arguments filed May 28, 2008 have been fully considered but they are not persuasive. The amendment has been entered. Claims 153-179 and 181-237 are pending. Claims 218-220 have been withdrawn from consideration as to a non-elected invention. Claims 153-179, 181-217 and 221-237 are examined herein.

Applicant's amendments to the claims and arguments have over come the rejections made in the office action mailed January 28, 2008 under 35 U.S.C. § 112, as lacking complete enablement. A scope rejection remains.

Applicant's amendments to the claims and arguments have over come the rejections made in the office action mailed January 28, 2008 under 35 U.S.C. § 102 and 103. At present the claims are all free of the prior art. At the time of filing the prior art did not teach or suggest culturing human ES cells in bFGF and TGF β 1 to maintain a pluripotent state.

Claim 229 is allowable as written.

Claims 157, 204, 205, 223 and 224 are objected to as depending on a rejected claim. These claims would be allowable if rewritten in independent form, incorporating all the limitations of the independent claim.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 153-156, 158-179, 181-203, 206-217, 221,222, 225-228 and 230-237 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for

a method of establishing a feeder cells-free human embryonic stem cell line which is maintained in an undifferentiated, pluripotent state, the method comprising (a) obtaining *ICM cells from a human blastocyst*, and (b) culturing said *ICM cells* under culturing conditions devoid of feeder cells and including a *human extracellular matrix* and a tissue culture medium supplemented with TGF β 1 and bFGF;

a method of propagating a human embryonic stem cell line in an undifferentiated, pluripotent and proliferative state under culturing conditions devoid of feeder cells, the method comprising culturing the human embryonic stem cell lines on a *human extracellular matrix* and tissue culture medium which comprises TGF β 1 and bFGF;

a method of establishing a xeno-free, feeder cells-free *mammalian* embryonic stem cell line which is maintained in an undifferentiated, pluripotent state, the method comprising (a) obtaining *ICM cells from a mammalian blastocyst*, and (b) culturing said *ICM cells* under culturing conditions devoid of feeder cells and including a xeno-contaminant-free *mammalian extracellular matrix* and a tissue culture medium devoid of xeno-contaminants supplemented with TGF β 1 and bFGF;

a method of propagating a *mammalian* embryonic stem cell line in an undifferentiated, pluripotent and proliferative state under culturing conditions devoid of feeder cells, the method comprising culturing the human embryonic stem cell lines on a

mammalian extracellular matrix and tissue culture medium which comprises TGF β 1 and bFGF;

A cell culture comprising undifferentiated, pluripotent and proliferative human embryonic stem cells *on a human extracellular matrix* in a culture medium comprising TGF β 1 and bFGF;

a xeno-free, feeder cell-free culture system comprising a *human extracellular matrix* devoid of xeno-contaminants and tissue culture medium devoid of xeno contaminants, said culture medium which comprises TGF β 1 and bFGF;

a method of maintaining human embryonic stem cells in an undifferentiated, pluripotent and proliferative state under culturing conditions devoid of feeder cells, the method comprising culturing the human embryonic stem cells under culturing conditions including a *human extracellular matrix* and tissue culture medium comprising TGF β 1 and bFGF, does not reasonably provide enablement for stem cells from human embryos, any species embryonic stem cell, growth on any type of matrix or cross-species extracellular matrices. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Mammalian embryonic stem cells, including human, are produced by first forming an embryo, and then isolating specific embryonic cells and culturing the embryonic cells to develop an embryonic stem cells. There are no embryonic or other stem cells in a mammalian embryo (see claim 153, as an example). Thus, the claims are not enabled as an embryo would not provide "stem cells." Further, mammalian embryonic stem cells

were known to be responsive to bFGF at the time of filing. Given the vast number of possible embryonic stem cells from all species, plant and animal as claimed, an undue amount of experimentation would be involved to determine the species and the particular matrix they would require for a culture of such stem cells to remain pluripotent, proliferative and undifferentiated (see claim 188, as an example).

The specification teaches several extracellular matrices (MEF, MatrigelTM, and foreskin fibroblast and bovine/human fibronectin) support the growth and pluripotency of hES cells (specification, page 40, lines 9-23). However, a matrix such as a culture dish is known to cause the formation of EB's, which are not pluripotent cells, but are cells of mesodermal, ectodermal and endodermal lineages (specification, page 33, lines 5-10). Thus, the generic term "matrix" is not enabled, but rather "extracellular matrix is. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Thus at the time of filing, the skilled artisan would have needed to engage in an undue amount of experimentation without a predictable degree of success to implement the invention as claimed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 158, 173 and 189 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 158, 173 and 189 include the term "substantially" which has not been given a definitive meaning in the art or in the specification. As such, the reader would not know the metes and bounds of these claims.

Claim 153 and 188 state "isolating stem cells of an embryo." However, stem cells do not exist in embryos, but are developed by culturing certain embryonic cell, such as ICM cells.

Claims 170, 171, 172, 174-177 and 188, state "embryonic stem cell line of a species" and a "species derived matrix," "species embryonic stem cell line" and a "species-derived matrix," and/or "species-derived serum." This terminology is confusing as all embryonic stem cell lines and all matrices are derived from some species. It is not clear what applicant means by species. The reader would be confused as to the correlation applicant is attempting to make through this terminology. In particular as applicant's claims appear to be related to xeno-contaminant free culture, this language is additionally confusing as it includes cross-species. There is no requirement that the claims contain ES cells, matrix or serum from the same species. Depending on the intention of the claim, applicant may consider rewriting the claims to indicate "same species."

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deborah Crouch, Ph.D. whose telephone number is (571)272-0727. The examiner can normally be reached on M-Fri, 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on 571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Deborah Crouch, Ph.D./
Primary Examiner, Art Unit 1632

September 15, 2008